

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: E. Fraley et al.

Serial No. 10/537,758

Filed: June 6, 2005

For: TYROSINE KINASE INHIBITORS

Art Unit: To Be AssignedExaminer: To Be Assigned

Commissioner for Patents  
P.O. Box 1450  
Alexandria, Virginia 22313-1450

**INFORMATION DISCLOSURE STATEMENT  
UNDER 37 CFR 1.97**

Sir:

1. In compliance with 37 C.F.R. 1.97, submitted on the attached form herewith is a list of patents, publications or other information which are requested to be made of record in this application. This Information Disclosure Statement is not an admission that any patent, publication or other information referred to herein is "prior art" for this invention. In accordance with 37 C.F.R. 1.97(h), the filing of this Information Disclosure Statement shall not be construed to be an admission that the information cited in the Statement is, or is considered to be, material to patentability as defined in 37 C.F.R. 1.56(b).
2. In accordance with 37 C.F.R. 1.97(g), the filing of this Information Disclosure Statement shall not be construed to mean that a search has been made.
3. Applicants respectfully request that the Examiner initial the attached form after reviewing the pertinence of each reference.
4. Pursuant to 37 C.F.R. 1.98 (a)(2)(ii), copies of each cited U.S. patent and each U.S. patent application publication are not enclosed herewith.

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450, on the date appearing below.

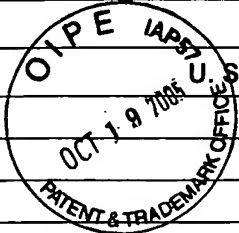
MERCK &amp; CO., INC.

By Marlene BrownDate 10/17/05

**INFORMATION DISCLOSURE STATEMENT**

5. Pursuant to 37 C.F.R. 1.98(d), copies of references listed on the attached form that were submitted to or cited by the Office in a related application upon which the instant application relies for an earlier filing date under 35 U.S.C. 120 are not enclosed. Related application(s) in which references were submitted to or cited by the Office are as follows:

RELATED APPLICATION		
U. S. SERIAL NUMBER	FILING DATE	MERCK CASE

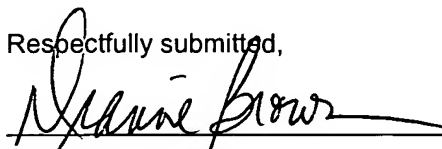


If this is inconvenient, additional copies will be submitted upon request.

6. In accordance with 37 C.F.R. 1.97, (check one)

- ☐ the attached information is filed within three months of the filing date of the captioned case.
- ☒ the attached information is filed more than three months after the filing date but prior to the mailing of a first Office Action on the merits.
- ☐ the attached information is filed before the mailing of a first Office action after the filing of a request for continued examination under §1.114.
- ☐ the attached information is being filed more than three months after the filing date and after the mailing of a first Office Action on the merits, but before the mailing date of a Final Action, Notice of Allowance, or an action that otherwise closes prosecution in the application. The enclosed authorization is therefore given to charge Deposit Account No. 13-2755 for the fee required under 37 C.F.R. 1.17(p).
- ☐ each item of information contained in this Information Disclosure Statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of this Statement.
- ☐ each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart application *and this communication was not received by any individual designated in §1.56(c) more than thirty days prior to the filing of the information disclosure statement.*
- ☐ no item of information contained in this Information Disclosure Statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, was known to any individual designated under 37 C.F.R. 1.56(c) more than three months prior to the filing of this Statement.

Respectfully submitted,



By: Dianne Brown

Attorney For Applicant(s)

Reg. No. 42,068

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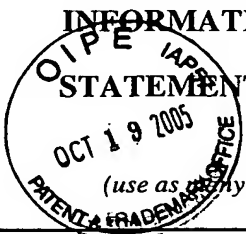
Patent Dept., RY60-30

P.O. Box 2000

Rahway, N.J. 07065-0907

(732)594- 1249

Date: October 17, 2005

Substitute for form 1449B/PTO <b>INFORMATION DISCLOSURE                  STATEMENT BY APPLICANT</b>  (use as many sheets as necessary)			<b>COMPLETE IF KNOWN</b>		
			Application Number	10/537,758	
			Filing Date	June 6, 2005	
			First Named Inventor	Mark E. Fraley	
			Group Art Unit	To Be Assigned	
			Examiner Name	To Be Assigned	
Sheet	1	of	1	Attorney Docket Number	20977P

NON PATENT LITERATURE DOCUMENTS		
Examiner Initials*	Cite No.	Include name of the author, title, date, page(s), volume-issue number(s) and place of publication.
	1	Bruggen, N.V., et al., "VEGF antagonism reduces edema formation and tissue damage after ischemia/reperfusion injury in the mouse brain", The Journal of Clinical Investigation, Vol. 104, pp 1613-1620 (1999)
	2	Deckers, M.M.L., et al., "Expression of Vascular Endothelial Growth Factors and Their Receptors during Osteoblast Differentiation", Endocrinology, Vol. 141, pp. 1667-1674 (2000)
	3	Fraley, M. E., et al., "Optimization of a Pyrazolo[1,5-]alpyrimidine Class of KDR Kinase Inhibitors: Improvements in Physical Properties Enhance Cellular Activity and Pharmacokinetics", Bioorganic & Medicinal Chemistry Letters, Vol 12, pp. 3537-3541 (2002)
	4	Fraley, M.E., et al., "Property-Based Design of KDR Kinase Inhibitors", Current Medicinal Chemistry, Vol. 11, pp. 709-719 (2004)
	5	Fraley, M.E., et al., "Synthesis and Initial SAR Studies of 3,6-Disubstituted Pyrazolo[1,5-]alpyrimidines: A New Class of KDR Kinase Inhibitors", Bioorganic & Medicinal Chemistry Letters, Vol. 12, pp. 2767-2770, (2002)
	6	Gerber, H.P., et al., "VEGF couples hypertrophic cartilage remodeling, ossification and angiogenesis during endochondral bone formation", Nature Medicine, Vol. 5, pp. 623-628 (1999)
	7	Greenberg, D.A., et al., "Angiogenesis and Stroke", Drug News Perspect, Vol. 11, pp. 265-270 (1998)
	8	Hasegawa, T., et al., "Intracortical osteoblastic osteosarcoma with oncogenic rickets", Skeletal Radiology, Vol. 28, pp. 41-45 (1999)
	9	Nakagawa, M., et al., "Vascular endothelial growth factor (VEGF) directly enhances osteoclastic bone resorption and survival of mature osteoclasts", FEBS Letters, Vol. 473, pp. 161-164 (2000)
	10	Paul, R. et al., "Src deficiency or blockade of Src activity in mice provides cerebral protection following stroke", Nature Medicine, Vol. 7, pp. 222-227 (2001)
	11	Rak, J., et a., "Mutant ras Oncogenes Upregulate VEGF/FPF Expression: Implications for Induction and Inhibition of Tumor Angiogenesis", Cancer Research, Vol. 55, pp. 4575-4580 (1995)

Examiner Signature		Date Considered	
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\*Examiner: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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